Appln. No. 09/806,837

Amdt. dated October 24, 2003

Reply to Office Action of July 24, 2003

## **Amendments to the Specification**

Page 4, after line 8, insert these paragraphs:

## BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1-a shows organ distribution of human serum albumin (HSA) conjugated with 10 to 12 cyclic oligopeptides recognizing the PDGF-receptor in normal rats.

Fig. 1-b shows organ distribution of human serum albumin (HSA) conjugated with 10 to 12 cyclic oligopeptides recognizing the PDGF-receptor in rats with liver fibrosis induced by bile duct ligation (3 weeks after the operation).

Fig. 1-c represents the organ distribution of unmodified HSA.

Fig. 2-a shows organ distribution of human serum albumin (HSA) conjugated with 10 to 12 cyclic oligopeptides recognizing the collagen type VI-receptor in normal rats.

Fig. 2-b shows organ distribution of human serum albumin (HSA) conjugated with 10 to 12 cyclic oligopeptides recognizing the collagen type VI-receptor in rats with liver fibrosis induced by bile duct ligation (3 weeks after the operation).

Fig. 3-a shows that after intravenous administration of modified protein, the albumin derivatives can be imuunhistochemically detected in a non-parenchymal cell type of the liver using a polyclonal antibody against albumin.

Fig. 3-b shows, as seen from the arrowheads, the modified albumin co-localizes with the marker for HSC (desmin).

Fig. 4 is a graph representing in vitro displacement of radiolabeled PDGF-BB from its receptor upon 3T3-fibroblasts by HSA-PDGF receptor-binding peptide conjugates (pPB-HSA, closed blocks), HSA (open blocks) or uncoupled PDGF-receptor binding peptides (pPB, open circles).

Fig. 5 is a graph of the organ distribution of radiolabeled M6Px-HSA in fibrotic rats (three weeks after bile duct ligation), 10 minutes after intravenous administration of the modified HSA.

Fig. 6 is a graph of the binding and uptake of radiolabeled  $M6P_{28}$ -HSA in human liver tissue at the reported temperatures.

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Page 4, amend the paragraph that starts at line 22 and bridges to page 5, through 2 to read:

Suitably, when the RRP is of a collagen type VI receptor, cytokine receptor such as TGFβ, TNFα and interleukin 1β, the cyclic portion of the cyclic peptide comprises at least the amino acid sequence RGD or KPT (lys-pro-thr) in the cyclic portion thereof. By way of example, the cyclic portion of the cyclic peptide comprises at least an amino acid sequence selected from X\*YRGDYX\* (Xaa(Xaa)<sub>n</sub>-arg-gly-asp-(Xaa)<sub>n</sub>-Xaa) and X\*YKPTYX\* (Xaa-(Xaa)<sub>n</sub>-lys-pro-thr-(Xaa)<sub>n</sub>-Xaa) wherein X\* represents the location of cyclisation and Y represents at least one amnio acid or a sequence of amino acids up to a length such that the receptor binding capacity of the cyclic peptide is retained. In an preferred embodiment, X\* represents the location of attachment to the carrier molecule. In an An embodiment illustrating the above, when the receptor agonist is of a collagen type VI receptor has a cyclic portion of the cyclic peptide comprising the amino acid sequence X\*GRGDSPX\* (Xaa-gly-arg-gly-asp-ser-pro-Xaa). Suitably, it will comprise the sequence -cysteine-glycine-arginine-glycine-aspartic aicd-serine-proline-cysteine. SEQ ID NO:1.

Page 5, amend the paragraph at lines 3-5 to read:

Suitably when the receptor agonist is of an interleukin 1 beta receptor, the cyclic peptide can comprise the amino acid sequence X\*DKPTLX\* (Xaa-asp-lys-pro-thr-lys-Xaa). SEQ ID NO:2.

Page 5, amend the paragraph at lines 6-14 to read:

Alternatively, when the receptor agonist is of PDGF receptor, the cyclic portion of the cyclid peptide can comprise the amino acid sequence X\*SRNLIDCX\* (Xaa-ser-arg-asn-leu-ile-asp-cys-Xaa), wherein X\* represents the location of cyclisation. <u>SEQ ID NO:3.</u> In a preferred emodiment X\* represents the location of attachment to the carrier molecule. Such a compound will bind to the PDGF receptor alha and beta subtypes. Suitably, it will comprise the sequence -cysteine-serine-arginine-asparagine-leucine-isoleucine-aspartic acid-cysteine.